REMARKS

Claims 1-6, 8-15, 20, 24-27, 30 and 31 are pending in the instant application. Claim 30 stands rejected under 35 USC § 112 for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims1-6, 8-9, 11-15, 20, 27 and 30 are rejected under USC § 103(a) as being unpatentable over Yu in view of Buck. Claim 10 is rejected under 35 USC § 103(a) as being unpatentable over Yu in view of Buck, and further in view of Katahira. Claims 24 and 25 are rejected under 35 USC § 103(a) as being unpatentable over Yu in view of Buck, and further in view of Obremski. Claim 26 is rejected under 35 USC § 103(a) as being unpatentable over Yu in view of Buck, and further in view of Pines. Claim 31 is rejected under 35 USC § 103(a) as being unpatentable over Yu in view of Buck, and further in view of Neild. The application has been amended. Claims 1 and 30 have been amended. Applicants respectfully submit that none of the amendments introduce new matter in contravention of 35 U.S.C. §132. Reconsideration is respectfully requested.

1. Claim 30 stands rejected under 35 USC § 112 for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 30 has now been amended such that the phrase "artificially high" has been replaced with the phrase "artificially-enriched abundance". The latter term is explained in detail on page 6 lines 15-32 of the instant application. Reconsideration and withdrawal of the rejection is respectfully requested.

2. Claims1-6, 8-9, 11-15, 20, 27 and 30 are rejected under USC § 103(a) as being unpatentable over Yu in view of Buck. The rejection is respectfully traversed.

The present invention discloses a liquid state assay method to monitor a physical or chemical change involving a chemical or biological species. The assay involves hyperpolarization of at least one NMR active nucleus of the assay reagent by a method selected from dynamic nuclear polarization and para-hydrogen-induced polarization. As stated in the description as filed on page 4 lines 27-29, the degree of hyperpolarisation of the

NMR active nucleus covered by the present invention is in excess of 0.1%. Claim 1 now explicitly quotes this hyperpolarisation value.

Yu teaches use of NMR spectroscopy in conjunction with an NMR active nucleus to analyze an assay but does not teach hyperpolarization of the NMR active nucleus.

Buck teaches photochemically-induced dynamic nuclear polarization (photo-CIDNP) for enhancing the NMR signal intensity in a binding assay. Buck does not explicitly teach any values for the degree of polarization achievable using photo-CIDNP, but a value can be estimated based on the figures. Figure 3 of Buck illustrates the best enhancement, in particular the peak present at just over 7ppm. As taught by Charles F Slichter in "Principles of Magnetic Resonance", Springer (Berlin & New York) 1990, 3rd Edition, pp. 4-9, To calculate the degree of polarization, the thermal equilibrium polarization is multiplied by the level of enhancement. For ^{1}H in a 360MHz spectrophotometer (in which photo-CIDNP measurements were carried out), the thermal equilibrium polarization is around 28ppm. Photo-CIDNP resulted in a peak measuring about 60mm, whereas the dark peak was about 3mm. Therefore the maximum enhancement achieved using photo-CIDNP according to Buck is around 20, resulting in a degree of polarization of 0.056% (0.000028 x 20 x 100), which is clearly below the minimum required by the present invention.

Therefore, the combination of the teachings of Yu and Buck does not lead to the present invention, which is therefore patentable over the prior art. Reconsideration and withdrawal of the rejection are respectfully requested.

3. Claim 10 is rejected under 35 USC § 103(a) as being unpatentable over Yu in view of Buck, and further in view of Katahira. The rejection is respectfully traversed.

As presented above, claims 1-6, 8-9, 11-15, 20, 27 and 30 are believed to be patentable over Yu in view of Buck. Katahira teaches that photo-CIDNP can be used in an NMR method to study base pairing. As discussed above, the technique of photo-CIDNP

does not result in the level of hyperpolarization required by the present invention. The teachings of Katahira therefore do not bring the teachings of Yu and Buck any closer to the method of claim 10 of the present invention.

Claim 10 of the present invention is therefore believed to be patentable over the prior art. Reconsideration and withdrawal of the rejection are respectfully requested.

4. Claims 24 and 25 are rejected under 35 USC § 103(a) as being unpatentable over Yu in view of Buck, and further in view of Obremski. The rejection is respectfully traversed.

As presented above, claims 1-6, 8-9, 11-15, 20, 27 and 30 are believed to be patentable over Yu in view of Buck. Obremski teaches a multiplexed or multispot assay and as such does nothing to bring the teachings of Yu in view of Buck any closer to the method of the present invention.

Furthermore, claims 24 and 25 both depend on claim 1 and are therefore believed to be patentable over the prior art. Reconsideration and withdrawal of the rejection are respectfully requested.

5. Claim 26 is rejected under 35 USC § 103(a) as being unpatentable over Yu in view of Buck, and further in view of Pines. The rejection is respectfully traversed.

As presented above, claims 1-6, 8-9, 11-15, 20, 27 and 30 are believed to be patentable over Yu in view of Buck. Pines teaches methods for using hyperpolarized noble gases in conjunction with NMR spectroscopy and MRI detection. In the method of Pines a sample is contacted with a hyperpolarized gas and the sample is then scanned by NMR and/or MRI to detect and NMR active nucleus in the sample. Pines does not teach hyperpolarization of at least one NMR active nucleus by either DNP or para-hydrogen-

induced hyperpolarization, wherein the NMR active nucleus one of ^{15}N, ^{19}F, ^{31}P, ^{1}H, ^{29}Si and ^{13}C, as required by the method of present claim 1.

Claim 26 is dependent upon claim 1 and therefore is believed to be patentable over the prior art for the reasons presented for claim 1 above. Reconsideration and withdrawal of the rejection are respectfully requested.

6. Claim 31 is rejected under 35 USC § 103(a) as being unpatentable over Yu in view of Buck, and further in view of Neild. The rejection is respectfully traversed.

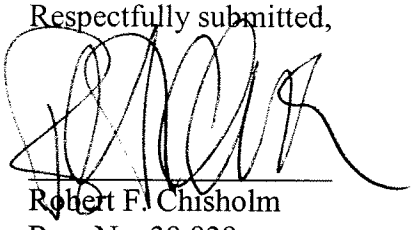
As presented above, claims 1-6, 8-9, 11-15, 20, 27 and 30 are believed to be patentable over Yu in view of Buck. Neild teaches that individual magnetic nuclei can interact with each other to produce additional splittings of the NMR peaks. There is no teaching in Neild relating to enhancement of the NMR signal by hyperpolarization as required by claim 1 of the present invention. Neild therefore does nothing to bring the combined teachings of Yu and Beck any closer to the presently-claimed method.

Claim 26 is dependent upon claim 1 and is therefore believed to be patentable over the prior art for the reasons presented for claim 1 above. Reconsideration and withdrawal of the rejection are respectfully requested.

Based on the amendments and remarks hereinabove, Applicants respectfully submit that the instant application, including claims 1, 3-6, 8-15, 20, 24-27, 30 and 31, is now in a condition for allowance. Favorable action is respectfully requested.

Any questions with respect to the foregoing may be directed to Applicants' undersigned counsel at the telephone number below.

Respectfully submitted,



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